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REACTIVITY OF β-ALKYLAMINO-SULPHONYL COMPOUNDS TOWARDS THIOPHENOLS

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Abstract—β-alkylamino-sulphone hydrochloride and methiodide derivatives react quantitatively with thiophenols, leading to the replacement of the alkylamino residue with the aryl-mercapto group.

Kinetic data indicate that the reaction proceeds through an elimination-addition mechanism, involving a pre-equilibrium for hydrochlorides.

For the two classes of compounds, different elimination mechanisms are suggested: an intramolecular one for hydrochlorides and a E_2 type mechanism, with a partially carbanionic character for methiodide derivatives.

The observed reactivity of both systems is then compared with that of the corresponding carbonyl compounds.

IN PREVIOUS work we studied qualitatively and quantitatively the reactivity of some β-alkylamino-ketones towards nucleophilic reactants.[2,3] In particular we investigated the exchange reaction of the alkyl-amino group of hydrochlorides and methiodides of some Mannich bases with thiols,[2,3]

$$\mathrm{Ar{-}CO{-}CH_2{-}CH_2{-}NR_2,\ (HCl\ and\ MeI)} \xrightarrow{\mathrm{HS{-}Ar'}} \mathrm{Ar{-}CO{-}CH_2{-}CH_2{-}S{-}Ar' + (NHR_2,\ HCl\ and\ NR_2Me,\ HI)}$$

and pointed out that these reactions occur with an elimination-addition mechanism.

In the present paper we deal with the reactivity of some aryl-β-alkylamino-sulphones, hydrochlorides and methiodides, since few examples are reported in the literature.[4] It was found that these compounds react with toluene-*p*-thiol in aqueous organic solvents as follows:

$$\underset{\text{I–VII and XIV–XVI}}{\mathrm{Ar{-}SO_2{-}(CH_2)_2{-}X}} + \mathrm{HS{-}C_6H_4{-}Me\text{-}}p \rightarrow \underset{\text{IX–XIII}}{\mathrm{Ar{-}SO_2{-}(CH_2)_2{-}S{-}C_6H_4{-}Me\text{-}}p} + \mathrm{HX}$$

	Ar	X		Ar
I	C_6H_5	$\overline{\mathrm{N{-}[CH_2]_4{-}CH_2}}$, HCl	IX	C_6H_5
II	C_6H_5	N $(Me)_2$, HCl	X	*p*-ClC_6H_4
III	C_6H_5	$\overline{\mathrm{N{-}[CH_2]_2{-}O{-}CH_2{-}CH_2}}$, HCl	XI	*m*-ClC_6H_4
IV	*p*-ClC_6H_4	$\overline{\mathrm{N{-}[CH_2]_4{-}CH_2}}$, HCl	XII	*p*-$NO_2C_6H_4$
V	*m*-ClC_6H_4	,, ,,	XIII	*p*-MeC_6H_4
VI	*p*-$NO_2C_6H_4$	,, ,,		
VII	*p*-MeC_6H_4	,, ,,		
XIV	C_6H_5	$\overline{\mathrm{N{-}[CH_2]_4{-}CH_2}}$, MeI		
XV	,,	N $(Me)_2$, MeI		
XVI	,,	$\overline{\mathrm{N{-}[CH_2]_2{-}O{-}CH_2{-}CH_2}}$, MeI		

In order to determine the effect of substitution of carbonyl with sulphonyl groups in organic molecules a comparison is made with the previously studied β-alkylaminoketones.

RESULTS

Hydrochlorides. β-alkylamino-sulphone hydrochlorides (I–VII) exchange their alkylamino group quantitatively with toluene-*p*-thiol in aqueous dioxan (Experimental).

In order to investigate the reaction mechanism, kinetic measurements were carried out at 90° ± 0·05 in buffered water-dioxan solutions (1 : 1)v. The reaction is first order with respect to the β-alkylamino-sulphones and zero order with respect to thiols. At fixed pa^{*}_{H} (see below) k is independent of the thiol used (Table 1), its concentration and the β-alkylamino-sulphone concentration. The first order rate constants were determined from a plot of log Do/D against time; this plot was linear over at least the second half life of the reaction. The velocity constants were correlated with the medium acidity. According to Bates[5a] the acidity in aqueous organic solvents is expressed by the unit pa^{*}_{H}. Bates[5b] pointed out that glass electrodes give a nearly theoretical response to the hydrogen ion concentration in water-ethanol (1 : 1)v, and a similar conclusion was obtained from water-dioxan.[6]

All measurements were carried out under experimental conditions. The pH-meter was standardized against aqueous buffered solutions prepared from NBS samples.

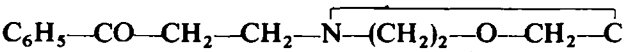
For β-alkylamino-sulphones (I, II and III), at low pa^{*}_{H}, k was found to increase rapidly as pa^{*}_{H} increases; then it became less sensitive, and finally unchanged from pa^{*}_{H} values (Table 2) approximately of 1·5–2·0 units higher than the β-amino-sulphone pKa.

In fact, in the solvent employed, a value of *ca* 0·8 pK_a units less than that measured in water at 25° is expected; as found for analogous compounds in solvents with the same dielectric constant.[7]

For the three investigated compounds the highest k-values clearly depend on the alkylamino group (Table 2).

At $pa^{*}_{\mathrm{H}} = 8{\cdot}0$, (+)phenyl-(α-methyl-β-dimethylamino) ethyl-sulphone hydrochloride (VIII) reaction yields racemic phenyl-(α-methyl-β-*p*-tolylthio) ethyl-sulphone; the unreacted hydrochloride shows no appreciable decay of its optical activity (Experimental).

Addition of sodium perchlorate in large excess over substrate provides no evidence of neutral salt effect at high pa^{*}_{H} (Table 3). In the investigated pa^{*}_{H} range, the rates of I and IV–VII were plotted against the Hammett[8] σ values[9] and gave a reasonable correlation: ρ values, at different pa^{*}_{H}, are nearly identical; their mean value is 1·3 ± 0·1 (Fig 1).

In order to compare the reactivity of β-aminoketones and β-aminosulphones, we investigated the reaction kinetics between  $C_6H_5{-}CO{-}CH_2{-}CH_2{-}\overline{N{-}(CH_2)_2{-}O{-}CH_2{-}CH_2}$ and toluene-*p*-thiol at different temperatures in buffered aqueous dioxan (1 : 1)v at $pa^{*}_{\mathrm{H}} = 9{\cdot}0$. The reaction rate constants had been previously determined in aqueous ethanol(1 : 1) v at 50°[2] and 35°.[3]

Temperature effect on reaction rate and activation parameters are reported in Table 4. These data also show that the solvent effect is small, the reaction occurring at

35° in aqueous dioxan ($k = 210 \times 10^{-6}$ sec^{-1}) and in aqueous ethanol ($k = 180 \times 10^{-6}$ sec^{-1}).[3]

At 90°, β-morpholinopropiophenone rate constant can be extrapolated from an Arrhenius type plot: the value obtained, $k = 300 \times 10^{-4}$ sec^{-1}, can be compared with the experimental phenyl-β-morpholinoethyl-sulphone k value, $0{\cdot}16 \times 10^{-4}$ sec^{-1}, measured at the same temperature.

Temperature effect and activation parameters for III are reported in Table 4.

Methiodides. β-alkylamino-sulphones methiodide derivatives (XIV, XV and XVI) and toluene-*p*-thiol yield sulphide (IX) quantitatively, in aqueous ethanol at 50° (Experimental).

Kinetic measurements were carried out at 50° in aqueous ethanol (1 : 1)v in a range of 2·5pa_H^* units for XIV. At fixed pa_H^* the reaction is strictly first order with respect to the substrate and zero order with respect to the thiol.

The reactivities of XIV, XV and XVI were also compared at $pa_H^* = 6{\cdot}5$.

Velocity constants for XIV and XV increase as pa_H^* increases and a plot of log k *vs* pa_H^* gives a straight line of unit slope; which means that the reaction is specifically base-catalysed.

Results are collected in Table 5 and Fig 2.

It is worthwhile to compare the pseudo first order rate constant of XVI at 50° and $pa_H^* = 6{\cdot}5$, $k = 530 \times 10^{-6}$ sec^{-1}, the medium difference being neglected, with that of the hydrochloride (III) extrapolated at the same temperature (Table 4: $k = 0{\cdot}48 \times 10^{-6}$ sec^{-1}). This value is strictly correct only at $pa_H^* = 9{\cdot}0$ (Table 4), but it can be considered as correct also at $pa_H^* = 6{\cdot}5$, for k does not change, pa_H^* changing in this range, as shown in Table 2.

A kinetic deuterium isotope effect $k_H/k_D = 3{\cdot}6$ was measured in aqueous ethanol for $C_6H_5{-}SO_2{-}CD_2{-}CH_2{-}N(Me)_2$, MeI (XVIII) at $pa_H^* = 6{\cdot}5$.

In our experimental conditions no isotope exchange between XVIII and the solvent was detected by ^{1}H NMR. The k_H/k_D value is nearly the same as the one observed for β-amino-ketones methiodide derivatives.[3]

From preliminary experiments carried out in our laboratory, it was found that a Hammett plot for β-piperidino-sulphone methiodides has a positive slope (ρ) close to 0·8.

DISCUSSION

From the above quoted results, it follows that the behaviour of β-amino-sulphones and β-amino-ketones is strictly analogous. Particularly for the hydrochlorides of the former, all the data can be rationalized according to the following reaction-pathway, as previously described for the latter:[2, 3]

$$\text{(A)}\quad Ar{-}SO_2{-}CH_2{-}CH_2{-}NR_2,HCl \rightleftharpoons Ar{-}SO_2{-}CH_2{-}CH_2{-}NR_2 + HCl$$

$$\text{(B)}\quad Ar{-}SO_2{-}CH_2{-}CH_2{-}NR_2 \rightleftharpoons Ar{-}SO_2{-}CH{=}CH_2 + HNR_2$$

$$\text{(C)}\quad Ar{-}SO_2{-}CH{=}CH_2 + Ar'{-}SH \rightarrow Ar{-}SO_2{-}CH_2{-}CH_2{-}S{-}Ar'$$

Stage (A) describes the equilibrium between the hydrochloride and its conjugate base. The relative concentrations of the two species is fixed by the buffer pa_H^*; (B) involves the elimination of alkylamino group (slow step) giving the vinyl-sulphone, which reacts, in its turn, rapidly and irreversibly with the thiol (C).

TABLE 1. RATE CONSTANTS FOR THE REACTION OF I, II, III AND THIOLS AT VARIOUS pa_H^* AT 90°

	pa_H^*	thiols	$k \times 10^6$ sec^{-1}
I	4·8	p-MeC$_6$H$_4$—SH	88
I	4·8	m-ClC$_6$H$_4$—SH	87
II	8·2	p-MeC$_6$H$_4$—SH	440
II	8·2	m-ClC$_6$H$_4$—SH	480
III	7·0	p-MeC$_6$H$_4$—SH	15
III	7·0	m-ClC$_6$H$_4$—SH	15

TABLE 2. RATE CONSTANTS FOR THE REACTION OF I, II, III WITH TOLUENE-p-THIOL AT VARIOUS pa_H^* AT 90°

pa_H^*	$k \times 10^6$ sec^{-1}		
	I	II	III
3·3			4·5
3·9	8·6	21	
4·3	34		
4·8	88	100	
5·8	140	180	13
7·0	230	400	15
8·2	260	440	15
9·0	260	420	16
10·0	280		
11·0	260		

TABLE 3. EFFECT OF NEUTRAL SALT ON THE REACTION OF I AND II WITH TOLUENE-p-THIOL AT pa_H^* = 9·0 AT 90°

Sodium perchlorate moles/l	$k \times 10^6$ sec^{-1}	
	I	II
0·00	260	420
0·05	268	416
0·10	277	432
0·25	269	422

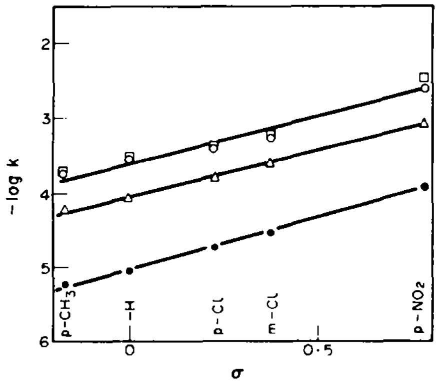


FIG 1. Hammett plot for the reaction between hydrochlorides (I), (IV)–(VII) and toluene-p-thiol at 90° and various pa_H^* (●, 3·9; △, 5·8; ○, 8·2; □, 9·0)

The latter is a "scavenger" of the equilibrium (B) and prevents the vinyl sulphone from reconverting into the starting material.

Table 2 clearly shows that the free base is the reacting species.

When it is fully available (high values of $pa_H^{\ddagger}$), k values do not change, $pa_H^{\ddagger}$ increasing. The highest k values of I. II and III follow roughly the basicity order[10] of the leaving amine group (in water, at 25°): Dimethyl-amine ($pK_a = 10·8$) $\simeq$ piperidine ($pK_a = 11·1$) $\gg$ morpholine ($pK_a = 8·4$).

The absence of base catalysis and the sequence of the rate constants maxima suggest that the proton-transfer in the elimination process (stage B) is an intramolecular one, possibly involving the assistance of a water molecule in the transition state.

For both β-amino-ketones and β-amino-sulphones, we found for ΔS^{**} a fairly high and negative value, indicating an order increase from the ground to the transition state, according to the proposed elimination mechanism.

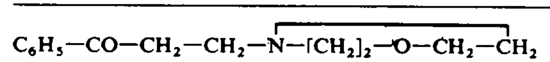
Sodium perchlorate addition to I and II, at high $pa_H^{\ddagger}$ values, gives no neutral salt effect, k being strictly constant at different electrolyte concentrations (Table 3). This demonstrates[11] that there is a negligible charge dislocation from the ground to the transition state, as expected for this concerted mechanism.

The Hammett ρ value 1·3 for amino-sulphones is unexpectedly identical to that of the amino-ketones, derived from measurements carried out under very different experimental conditions.[3] Nevertheless, the ρ values support the hypothesis of an analogous, non synchronous elimination mechanism for both classes of compounds.

The results obtained in the same solvent for III and β-morpholinopropiophenone demonstrate that the β-amino-ketones reactivity towards toluene-p-thiol is approximately two thousand times higher than the β-amino-sulphones.

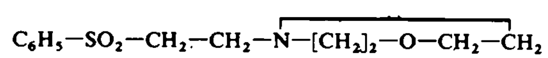
Our results suggest that the difference in reactivity is due to the difference in acidity between the protons α to the sulphonyl and to the carbonyl group; the difference is indeed of three pK_a units.[12,13]

TABLE 4. RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE REACTION OF β-MORPHOLINOPROPIOPHENONE AND III WITH TOLUENE-p-THIOL IN AQUEOUS DIOXAN AT $pa_H^{\ddagger} = 9·0$



$C_6H_5{-}CO{-}CH_2{-}CH_2{-}N{-}[CH_2]_2{-}O{-}CH_2{-}CH_2$

$k \times 10^6$ sec^{-1}	t°	ΔH^{**} ($k$cal mole^{-1})	ΔS^{**} (e.u.)
210	35·0	18·7 ± 0·4	−16·0 ± 1·5
350	40·0		
520	44·7		
810	49·2		
1400	54·4		



$C_6H_5{-}SO_2{-}CH_2{-}CH_2{-}N{-}[CH_2]_2{-}O{-}CH_2{-}CH_2$

$k \times 10^6$ sec^{-1}	t°	ΔH^{**} ($k$cal mole^{-1})	ΔS^{**} (e.u.)
3·8	73·1	19·6 ± 0·4	−25·6 ± 1·5
4.4	75·6		
8·4	83·3		
16·0	90·0		
18·0	92·1		

For the methiodides the exchange reaction may be described as follows:

(B′) $C_6H_5-SO_2-CH_2-CH_2-NR_2, MeI \rightarrow C_6H_5-SO_2-CH=CH_2 + MeNR_2, HI$

(C′) $C_6H_5-SO_2-CH=CH_2 + HS-Ar \rightarrow C_6H_5-SO_2-CH_2-CH_2-S-Ar$

The outstanding differences between the behaviour of the methiodides and the hydrochlorides are:

(1) Absence of a preequilibrium as in (A);

(2) The intermediate vinyl-sulphone cannot reconvert into the starting material.

The methiodides of both β-amino-ketones[3] and β-amino-sulphones are much more reactive towards thiols than the corresponding free bases. This relates to a different elimination mechanism involved in the rate determining stages (B) and (B′).

Our experimental results, particularly specific base catalysis and deuterium isotope effect, agree with an E_2 type elimination mechanism operating in (B′).

The anticipated Hammett ρ value and the experimental ratio $k_H/k_D = 3{\cdot}6$, together with the small leaving group effect (Table 5) clearly indicate that considerable carbanionic character[14,15] is involved in the transition state "E_{1CB} like" of the elimination process B′, although one should be cautious[16] in drawing even semiquantitative conclusions about transition state structure from single measurements of isotope effects.

TABLE 5. RATE CONSTANTS FOR THE REACTION OF METHIODIDES (XIV, XV and XVI) WITH TOLUENE-*p*-THIOL AT 50°

pa_H^*	$k \times 10^6\ sec^{-1}$		
	XIV	XV	XVI
4·9	13	14	
5·2	23		
5·5	53	45	
5·9	120	190	
6·5	390	530	530
7·0	1200		
7·5	3400		

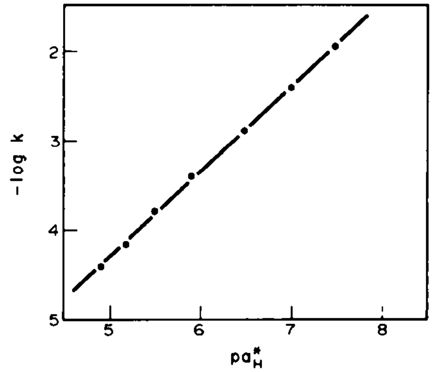


FIG 2. Plot of log k vs pa_H^* for the reaction between methiodide (XIV) and toluene-p-thiol at 50°

EXPERIMENTAL

M.ps are uncorrected. ^{1}H NMR spectra were obtained for 10% w/v solns in D_2O (DSS was used as internal standard) with a Jeolco C-60 H L instrument. UV spectra were determined with a Beckman D.U. spectrophotometer. Specific rotations were measured by a Bendix N.P.L. Automatic Polarimeter. For pH measurements a glass electrode was adopted in connection with a Beckmann Zeromatic II pH meter; a calomel electrode was used as standard and microanalyses were carried out with an F & M 185 C.H.N. analyzer.

TABLE 6. ARYL-β-ALKYLAMINOETHYL-SULPHONE HYDROCHLORIDES AND REACTION PRODUCTS WITH TOLUENE-*p*-THIOL. PHYSICAL CONSTANTS

	Hydrochlorides				Products sulphides	
	Ar	NR_2	m.p.	λ_{max} (mμ)* (log ε) in water		m.p.
I[a]	C_6H_5	$\overline{\mathrm{N}-[\mathrm{CH}_2]_4-\mathrm{C}}\mathrm{H}_2$	220–222°	266 (3·09)	IX[h]	90–92°
II[b]	C_6H_5	N(Me)$_2$,	180–182°	266 (3·08)	„	„
III[c]	C_6H_5	$\overline{\mathrm{N}-[\mathrm{CH}_2]_2-\mathrm{O}-\mathrm{CH}_2-\mathrm{C}}\mathrm{H}_2$	237–238°	266 (3·08)	„	„
IV[d]	*p*-ClC_6H_4	$\overline{\mathrm{N}-[\mathrm{CH}_2]_4-\mathrm{C}}\mathrm{H}_2$	221–222°	268 (3·18)	X[i]	125–126°
V[e]	*m*-ClC_6H_4	$\overline{\mathrm{N}-[\mathrm{CH}_2]_4-\mathrm{C}}\mathrm{H}_2$	216–218°	276 (3·13)	XI[j]	88–89°
VI[f]	*p*-$NO_2C_6H_4$	$\overline{\mathrm{N}-[\mathrm{CH}_2]_4-\mathrm{C}}\mathrm{H}_2$	222–224°	250 (4·13)	XII[k]	123–125°
VII[g]	*p*-MeC_6H_4	$\overline{\mathrm{N}-[\mathrm{CH}_2]_4-\mathrm{C}}\mathrm{H}_2$	236–238°	264 (3·05)	XIII[l]	83–84°

[*] λ_{max} Values are those used for quantitative measurements.

[a] Lit.: 205–206°—O. Achmatowicz, E. Maruszewka-Wieczorkowska and Y. Michailski, *Roczniki Chem.* **29**, 1029 (1955); *Chem. Abstr.* **50**, 120464h (1956)

[b] Found: C, 47·97; H, 6·43; N, 5·66. $C_{10}H_{16}ClNO_2S$ requires: C, 48·08; H, 6·45; N, 5·61%.

[c] Lit.: 226–228°. Jushih Tsung and Ju-Yünchi, *Hua Hsüen Pao* **26**, 31 (1960); *Chem. Abstr.* **55**, 17635e (1961)

[d] Found: C, 48·39; H, 6·01; N, 4·40. $C_{13}H_{19}Cl_2NO_2S$ requires: C, 48·14; H, 5·91; N, 4·32%.

[e] Found: C, 48·10; H, 6·03; N, 4·40. $C_{13}H_{19}Cl_2NO_2S$ requires: C, 48·14; H, 5·91; N, 4·32%.

[f] Lit.: 218–219°: M. Protiva, M. Borovička and E. Hachová, *Čekoslov. Farm.* **8**, 200 (1959); *Chem. Abstr.* **54**, 6609e (1960)

[g] Lit.: 229–230°—Farbwerke Hoechst Akt.-Ges. (J. Heyna and W. Riemenschneider). Ger. 1,064,055. Aug. 27, 1959 (Cl. 12); *Chem. Abstr.* **55**, 13450f (1961)

[h] Lit.: 95–96°—A. H. Ford-Moore, R. A. Peters and R. W. Wakelin, *J. Chem. Soc.* 1754 (1949)

The sulphide product of the reaction between I and *m*-chlorobenzenethiol has m.p. 96–97° (from EtOH): Found: C, 53·30; H, 4·12. $C_{14}H_{13}ClO_2S_2$ requires: C, 53·76; H, 4·19%.

[i] Found: C, 55·35; H, 4·84. $C_{15}H_{15}ClO_2S_2$ requires: C, 55·11; H, 4·63%.

[j] Found: C, 55·27; H, 4·52. $C_{15}H_{15}ClO_2S_2$ requires: C, 55·11; H, 4·63%.

[k] Found: C, 53·20; H, 4·51; N, 4·12. $C_{15}H_{15}NO_4S_2$ requires: C, 53·39; H, 4·48; N, 4·15%.

[l] W. Reppe, *Liebigs Ann.* **601**, 111 (1956).

Aryl-β-alkylaminoethyl-sulphone hydrochlorides (I–VII)

The bases related to I–VII were prepared by reacting the aryl-β-chloroethyl-sulphones*[17] with suitable amines. Compounds I–VII were obtained in the usual way and purified by crystallization from EtOH (Table 6). The ^{1}H NMR spectrum of II gave: τ 2·10 (5 H, m, aromatic H); 6·25 (4 H, m, CH_2—CH_2); 6·98 (6 H (NMe_2).

Phenyl-(α,α'-dideutero-β-dimethylamino)ethyl-sulphone hydrochloride and methiodide (XVII)

A complete H-D exchange in α position to the sulphonyl group occurs when a 1 M soln of the base of II in D_2O—EtOD (1:1)v is left for two days at room temp. The hydrochloride obtained in the usual way has m.p. = 177–178° (Found: C, 48·56; H, 6·54; N, 5·64. $C_{10}H_{14}D_2ClNO_2S$ requires: C, 47·72; H + D, 7·21: N, 5·56%).

The ^{1}H NMR spectrum of the hydrochloride gave: τ 2·10 (5 H, m, aromatic H); 6·42 (2 H, s, CD_2—CH_2); 7·02 (6 H, s, NMe_2).

The methiodide was obtained as usual (m.p. = 174–175°). (Found: C, 36·84; H, 4·94; N, 4·02. $C_{11}H_{16}D_2INO_2S$ requires: C, 36·98; H + D, 5·63; N, 3·92%).

Aryl-β-p-tolylthioethyl-sulphones (IX–XIII)

Method A. A water-dioxan soln (1:1)v of the hydrochlorides (I–VII) and toluene-*p*-thiol were heated under reflux for 24 hr.

The products (IX–XIII) were isolated quantitatively and identified (Table 6).

Method B. A water-EtOH soln (1:1)v of methiodides (XIV–XVI) and toluene-*p*-thiol were heated under reflux for 5 hr. The product (IX) was obtained quantitatively. The reaction between XIV and thiophenol was carried out in the same way.[18]

(+)Phenyl-(α-methyl-β-dimethylamino)ethyl-sulphone hydrochloride (VIII)

An equimolar amount of *n*-BuLi in ether titrated soln[19] was added slowly to a well-stirred soln of phenyl-β-dimethylaminoethyl-sulphone in dry ether at −20°, under N_2. When *n*-BuLi addition was complete, the mixture was stirred for 1 hr at −10° and an equimolar amount of MeI slowly added. The mixture was stirred at room temp for 2 hr and poured into ice water. The organic layer was washed twice with water and then dried (Na_2SO_4).

The (±)phenyl-(α-methyl-β-dimethylamino)ethyl-sulphone hydrochloride was obtained in the usual way and crystallized from abs EtOH, m.p. = 214–216°: yield 45%. (Found: C, 49·85; H, 7·00; N, 5·35. $C_{11}H_{18}ClNO_2S$ requires: C, 50·08; H, 6·88; N, 5·31%); ^{1}H NMR spectrum gave: τ 2·15 (5 H, m, aromatic); 6·25 (3 H, m, CH—CH_2); 6·95 (6 H, s, NMe_2); 8·65 (3 H, d, Me).

TABLE 7. PHENYL-β-ALKYLAMINOETHYL-SULPHONE METHIODIDES, PHYSICAL CONSTANTS

	NR_2	m.p.	λ_{max}(mμ) (log ε in water) (log ε)
XIV[4]	$\overline{N-[CH_2]_4-CH_2}$	170–172°	266 (3·08)
XV[a]	$N(Me)_2$	180–182°	266 (3·08)
XVI[b]	$\overline{N-[CH_2]_2-O-CH_2-CH_2}$	172–174°	266 (3·08)

[a] Found: C, 37·22; H, 5·04; N, 4·10. $C_{11}H_{18}JNO_2S$ requires: C, 37·18; H, 5·11; N, 3·94%.

[b] Found: C, 38·95; H, 4·87; N, 3·38. $C_{13}H_{20}JNO_3S$ requires: C, 39·29; H, 5·07; N, 3·52%.

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* The aryl-β-chloroethyl-sulphones were obtained as reported.[17] *m*-Chlorophenyl-β-chloroethyl-sulphone was prepared in a similar way and has m.p. = 57–58° from EtOH. (Found: C, 40·25; H, 3·15. $C_8H_8Cl_2O_2S$ requires: C, 40·18; H, 3·37%).

TABLE 8. REACTION BETWEEN I AND TOLUENE-*p*-THIOL AT $pa_H^* = 9{\cdot}0$ AND 90°

Time, sec.	Optical Density, D at 266 mμ	$k \times 10^6$ sec^{-1}
120	0·545	—
960	0·430	251
1780	0·345	253
2680	0·275	256
3600	0·215	255
4500	0·170	261
5900	0·115	263
		Av. 256

k from slope 260×10^{-6} sec^{-1}

To a soln in abs EtOH of (±)phenyl-(α-methyl-β-dimethylamino)ethyl-sulphone an equimolar amount of D(−)-dibenzoyl-tartaric acid was added and the precipitated salt recrystallized from EtOH, m.p. = 125–127°. (Found: C, 58·29; H, 5·09; N, 2·42. $C_{29}H_{32}O_{10}NS{\cdot}H_2O$ requires: C, 57·71; H, 5·51; N, 2·32%).

From the salt (+)phenyl-(α-methyl-β-dimethylamino)ethyl-sulphone was obtained: $[\alpha]_D = 3{\cdot}8$ (*c*, 3 EtOH). The hydrochloride (VIII) had m.p. 209–211°, $[\alpha]_D = 1{\cdot}4$ (*c*, 3·28 EtOH). (Found: C, 50·53; H, 6·98; N, 5·40. $C_{11}H_{18}NO_2S$ requires: C, 50·08; H, 6·88; N, 5·31%).

(±)*Phenyl-(α-methyl-β-p-tolylthio)ethyl-sulphone*

A water-dioxan soln (1:1)v of VIII and toluene-*p*-thiol were heated under reflux for 24 hr ($pa_H^* = 8{\cdot}0$); the product was then precipitated and crystallized from EtOH, m.p. = 59–60°, yield 10%. (Found: C, 62·62; H, 5·97. $C_{16}H_{18}S_2O_2$ requires: C, 62·71; H, 5·92%); no optical rotation was observed for this compound; and the unreacted hydrochloride does not exhibit racemisation.

Potentiometric titrations. 25° thermostated solns, containing 2×10^{-4} moles of I, II and III in 100 ml water, were titrated with 0·1 N NaOH with a Beckmann Zeromatic II pH-meter. In order to keep the ionic strength constant, 10^{-2} moles of $NaNO_3$ had been added.

For acid dissociation constants the following values were obtained:
$pK_a = 7{\cdot}3$ for I; 7·04 for II; 4·8 for III. P. Zuman *et al.*[4] found $pK_a = 7{\cdot}06$ for I.

Kinetics. The reaction velocities were measured according to the technique previously described.[1–3] The reaction components were separated by extraction with diethyl ether (hydrochlorides) or methylene chloride (methiodides) before spectrophotometric reading and the concentration of β-amino-sulphones (hydrochlorides and methiodides) was followed by the change in optical density at the reported λ_{max} values (Tables 6 and 7). One example of decay of absorbance with time is reported in Table 8.

All materials for kinetic runs were reagent grade quality.

ΔH^{**} and ΔS^{**} for the exchange reaction (Table 4) were calculated by a standard method.[20]

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